REMARKS

Claims 29-47 have been canceled without prejudice or disclaimer. Claims 48-76 have been added and therefore are pending in the present application. Claims 48-76 are supported by the specification, including the original claims. Claims 48-59 and 63-73 read on the elected invention.

The specification has been amended to provide that "Avicel" is a registered trademark.

It is respectfully submitted that the present amendment presents no new issues or new matter and places this case in condition for allowance. Reconsideration of the application in view of the above amendments and the following remarks is requested.

I. The Restriction and Election of Species Requirements

The Office maintained the restriction and election of species requirements. Both requirements are traversed for the reasons of record.

The Office states that "[t]he phrase 'an amino acid sequence' reads broadly on any dipeptide of the sequence having 50% identity to the sequence 34-174 of SEQ ID NO: 2." This is not a reasonable interpretation of the claims, and contrary to how this phrase would be interpreted by persons skilled in the art. Under the Office's interpretation, almost all sequences are 100% identical.

Moreover, the Office's interpretation is not consistent with the specification. The specification describes at pages 6 and 7 how to determine % identity between two amino acid sequences. For example, it discloses that FIG2 of *Saccharomyces cerevisiae* (Swiss-Prt No. p25653) (a copy of which is attached hereto) is 28.7% identical to the sequence of amino acids 34-174 of SEQ ID NO: 2. Under the Office's interpretation, these two sequences would be 100% identical because FIG2 comprises the amino acids Val-Val at positions 13-14 which are identical to the amino acids at positions 58-59 of SEQ ID NO: 2.

The Office Action also stated that "The carbohydrate-binding domain, as broadly claimed, does not represent an advance over the art (see Levy et al., "Cellulose-binding domains-Biotechnological applications", cited in search report) and hence there is no unity of invention." This is respectfully traversed.

The Office provides no evidence that the carbohydrate-binding modules disclosed in Levy et al. have an amino acid sequence which is at least 80% identical to the sequence of amino acids 34-174 of SEQ ID NO: 2. As described in the specification, the carbohydrate-binding module (see page 3, lines 9-10) from *Pseudoplectania nigrella* is "the first known member of a new family of CBM's" (see page 3, lines 9-10). Thus, the carbohydrate-binding modules described in Levy et al.

do not have an amino sequence which is homologous to the sequence of amino acids 34-174 of SEQ ID NO: 2.

For the foregoing reasons, Applicants submit that the restriction and election of species requirements are improper, and respectfully request reconsideration and withdrawal thereof.

II. The Objection to the Specification

The Office objected to the specification because the trademark Avicel has not been capitalized.

The specification has been amended to add a registration mark after each occurrence of Avicel. Applicants therefore submit that the proprietary nature of the mark is respected.

III. The Objection to Claim 34

The Office objected to claim 34 because a period is missing at the end of the sentence. Claim 34 has been canceled without prejudice or disclaimer. Therefore, this objection is rendered moot.

IV. The Rejection of Claim 34 under 35 U.S.C. 112

Claim 34 is rejected under 35 U.S.C. 112 as being indefinite because "it is unclear whether the phrase 'which has carbohydrate-binding module activity' in line 2 is meant to limit the term 'fragment' in line 1 or rather pertains to the term 'the sequence of amino acids 34-174 of SEQ ID NO: 2." This rejection is respectfully traversed.

Applicants submit that this phrase is clear to persons skilled in the art, and would be understood to mean that the fragment has carbohydrate-binding module activity.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 112. Applicants respectfully request reconsideration and withdrawal of the rejection.

V. The Rejection of Claims 29-39 and 43-44 under 35 U.S.C. 112

Claims 29-39 and 43-44 are rejected under 35 U.S.C. 112 as failing to comply with the written description requirement. This rejection is respectfully traversed.

It is well settled that "[t]he test for determining compliance with the written description requirement is whether the disclosure of the application as originally filed reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter ..." *In re Kaslow*, 217 USPQ 1089, 1096 (Fed. Cir. 1983). The written description as filed is presumed to be

adequate, unless or until sufficient evidence or reasoning to the contrary has been presented by the examiner to rebut the presumption. See *In re Marzocchi*, 169 U.S.P.Q. 367 (C.C.P.A. 1971).

As set forth in Federal Circuit decisions, a specification complies with the written description requirement if it provides "a precise definition, such as by structure, formula, chemical name, or physical properties of the claimed subject matter sufficient to distinguish it from other materials." *See*, *e.g.*, *University of California v. Eli Lilly and Co.*, 43 U.S.P.Q.2d 1398, 1404 (Fed. Cir. 1997); *Enzo Biochem v. Gen-Probe Inc.*, 63 U.S.P.Q.2d 1609, 1613 (Fed. Cir. 2002).

Moreover, the Written Description Training Materials published by the USPTO on March 25, 2008 provides guidance in applying the written description requirement. Particularly relevant to the instant application is Example 11, "Percent Identity" and more specifically, Example 11B "Art-Recognized Structure-Function Correlation Present." Example 11B provides "Claim 2" which is a claim to an isolated nucleic acid sequence that encodes a polypeptide with at least 85% amino acid sequence identity to SEQ ID NO: 2; wherein the polypeptide has activity Y. The specification of Example 11B discloses the reduction to practice of only a single species that encodes SEQ ID NO: 2 and has activity Y, *i.e.*, nucleic acid SEQ ID NO: 1, but the specification does not teach which 15% of the amino acids will vary from SEQ ID NO: 2, nor any other polypeptides with 85% identity to SEQ ID NO: 2 that have activity Y. However, the knowledge in the art of the genetic code would allow one skilled in the art, with the aid of a computer, to list all of the nucleotide sequences capable of encoding a polypeptide with at least 85% identity to SEQ ID NO: 2, thus identifying all polypeptides having at least 85% identity to SEQ ID NO: 2. Further, Example 11B provides that the specification identifies two domains responsible for the activity Y, *i.e.*, a binding domain and a catalytic domain, and predicts that conservative mutations in these domains will result in the protein having activity Y, and those of ordinary skill in the art would expect that many of the conservative substitutions would result in a protein having the required activity. Additionally, substitutions outside of the functional domains were predicted to have little effect on activity Y. Thus, a correlation exists between the function of the claimed protein and the structure of the disclosed binding and catalytic domains. The conclusion is that the written description requirement is satisfied for Claim 2 of Example 11B.

Applicants respectfully submit that the claims of the instant application comply with the written description requirement under 35 U.S.C. 112, first paragraph.

The claimed invention is directed to carbohydrate-binding modules, which (a) have a sequence which has at least 90% identity with the sequence of amino acids 34-174 of SEQ ID NO: 2; (b) are encoded by a DNA sequence that hybridizes to the DNA sequence of nucleotides 109-531 of SEQ ID NO: 1 under high stringency conditions; or (c) are a fragment of the

sequence of amino acids 34-174 of SEQ ID NO: 2. Thus, the claimed polypeptides are structurally similar.

It would be routine for persons of ordinary skill in the art to identify each amino acid sequence which falls within the 90% sequence identity recitation and to test the polypeptide for carbohydrate-binding module activity. The specification discloses a computer program for determining percent identity at pages 6 and 7.

Furthermore, carbohydrate-binding modules are well characterized and those skilled in the art can recognize the conserved regions among carbohydrate-binding modules. Just as one skilled in the art can recognize mutations to the catalytic and binding domains and substitutions outside of the catalytic and binding domains of SEQ ID NO: 2 in Example 11B which would result in a polypeptide having activity Y, persons skilled in the art also can recognize mutations to the polypeptide of SEQ ID NO: 2, which would result in a polypeptide having carbohydrate-binding module activity.

Applicants respectfully submit that the claims of the instant application meet the requirement for written description under 35 U.S.C. 112, first paragraph, by disclosing relevant, identifying characteristics, *e.g.*, the structure of SEQ ID NO: 2, and by functional characteristics, *i.e.*, carbohydrate-binding module activity, coupled with the known correlation between function and structure. Given the high degree of identity recited in the claims, a high degree of predictability exists as to the structure and function of polypeptide falling within the claims.

Moreover, it is well established in the art that the definition of a genus of genes encoding polypeptides having an enzyme activity of interest is accomplished by using structural features that show the relatedness of the genes and their encoded products. For decades the scientific community has employed three structural features to define the relatedness of genes and their products. The three structural features are (1) percent identity of the amino acid sequences encoded by the genes, (2) percent homology of the nucleic acid sequences of the genes, and (3) nucleic acid hybridizations under defined stringent conditions to identify complementary strands of genes encoding the same or similar enzyme or protein function. These structural features have been used to predict the function of polypeptides encoded by novel genes, and to place them in an existing genus.

These structural features are highly predictive of protein function. In particular, proteins that share 80% amino acid identity are known to possess the same catalytic/biochemical function. In fact, 80% identity is a conservative criterion for judging functional similarity. A long history of structure-function studies has demonstrated that single domain proteins that share substantial similarity (and >30% identity) over their entire length (>80 residues) without

introduction of numerous gaps are almost certainly homologous (derive from a common evolutionary ancestor) and share the same three-dimensional structure (see Marti-Renom et al., 2000, *Annu. Rev. Biophys. Biomol. Struct.* 29:291–325 (a copy of which is attached hereto)). At the 80-90% level of amino acid identity, orthologous enzymes in related species are virtually guaranteed to share the same catalytic function and substrate specificity. A simple search of any public database using the criteria above for a reference protein of interest will prove that there is a definitive relationship between protein function and % identity at the amino acid level.

Moreover, Guo et al., 2004, *Proc. Nat. Acad Sci USA* 101: 9205-9210 (a copy of which is attached hereto), observed that various residues of a protein are differentially sensitive to substitutions, and that tolerance of the entire protein to random change can be characterized by a probabilistic relationship termed the "x-factor." The x-factor is broadly defined as the probability that a random amino acid replacement will lead to functional inactivation. Moreover, they determined the x-factor to be 34% +/- 6%. Contrary to the Office's contention that random (even conservative) changes in a protein in the absence of structural information would adversely affect activity, the findings of Guo et al. support the contrary, *i.e.*, that proteins are generally tolerant to random amino acid substitutions, and the probability of destroying protein function is small.

Makiewicz et al., 1994, *J. Mol. Biol.* 240: 421-433 (a copy of which is attached hereto), examined 12 or 13 different amino acid substitutions at each residue across 90% of the 360 amino acid *E. coli lac* repressor protein. Reanalysis of their data by Guo et al. (2004) revealed an x-factor value of 34% which is identical to the value for random inactivation of human 3-methyladenine DNA glycosylase studied by Guo et al. Axe et al., 1998, *Biochem.* 37: 7157-7166 (a copy of which is attached hereto), found that 95% of randomly introduced single amino acid substitutions did not lead to inactivated ribonuclease enzyme. Rennell et al., 1991, *J. Mol. Biol.* 222: 67-88 (a copy of which is attached hereto), found that approximately 84% of amino acid substitutions in T4 lysozyme did not cause inactivation.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 112. Applicants respectfully request reconsideration and withdrawal of the rejection.

VI. The Rejection of Claims 29-39 and 43-44 under 35 U.S.C. 102

Claims 29-38 and 43 are rejected under 35 U.S.C. 102(b) as anticipated by Bourne and Henrissat (Current Opinion in Structural Biology, 2001, 11: 593-600). Claims 29-39 and 43-44 are rejected under 35 U.S.C. 102(b) as anticipated by Levy et al. (Biotechnology Advances, 2002 20: 191-213). Both rejections are respectfully traversed.

Both rejections are based on an incorrect construction of the claims. As explained above, the claim construction provided in the Office Action is unreasonable and contrary to how this phrase would be interpreted by persons skilled in the art. Under the Office's interpretation, almost all sequences are 100% identical.

Bourne et al. and Levy et al. disclose carbohydrate-binding modules from various enzymes. However, neither reference disclose a carbohydrate-binding module which (a) has a sequence which has at least 90% identity with the sequence of amino acids 34-174 of SEQ ID NO: 2; (b) is encoded by a DNA sequence that hybridizes to the DNA sequence of nucleotides 109-531 of SEQ ID NO: 1 under high stringency conditions; or (c) is a fragment of the sequence of amino acids 34-174 of SEQ ID NO: 2, as claimed herein.

For the foregoing reasons, Applicants submit that the claims overcome these rejections under 35 U.S.C. 102. Applicants respectfully request reconsideration and withdrawal of the rejections.

VII. Conclusion

In view of the above, it is respectfully submitted that all claims are in condition for allowance. Early action to that end is respectfully requested. The Examiner is hereby invited to contact the undersigned by telephone if there are any questions concerning this amendment or application.

Please charge all required fees to Novozymes North America, Inc.'s Deposit Account No. 50-1701 at the time of electronic filing. The USPTO is authorized to charge this Deposit Account should any additional fees be due.

Respectfully submitted,

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